

## Appendix 2

Lima Peru 3-5 September 2019



## GLOBAL FUNGAL INFECTION FORUM 4 NEGLECTED FUNGAL SKIN TROPICAL DISEASES

95/95  
BY 2025



## Neglected fungal skin tropical diseases

### Mycetoma in South America

The endemic Implantation (subcutaneous) mycoses are a frequent health problem in tropical and subtropical areas of most of the Latin America countries.

Mycetoma is one example of a severe implantation mycosis. Mycetoma is a chronic infectious disease, which can be caused by different species of fungus (eumycetoma) or by aerobic filamentous bacteria (actinomycetoma). According to the South American literature, mycetoma is the third most prevalent endemic implantation mycoses in the region, especially among low socioeconomic adult males living in rural areas from Argentina, Brazil, Colombia and Venezuela. Similarly, to the other endemic regions, mycetoma more frequently affects individuals who encounter frequent and direct contact with the soil, especially those in rural areas, such as farmers, hunters, herdsman and other outdoor activities. Actinomycetoma, usually caused by *Nocardia* species complex are more commonly found in South America than eumycetoma but overall, the prevalence of eumycetoma is rising with *Madurella* spp. and *S. apiospermum* (*Pseudallescheria boydii*) as the major etiologic agents. Less frequently, *Exophiala jeanselmei*, *Acremonium* spp, *Medicopsis romeroi* (*Pyrenochaeta romeroi*), *Biatrispora mackinnonii* (*P. mackinnonii*), and *Pseudochaetosphaeronema larense* (*Chaetosphaeronema larense*) have been also reported from patients with eumycetoma in Latin America.

In Brazil, combined retrospective data from a single center showed that from 1944 – 2000, 222 mycetoma cases were reported. Of the treated cases, the proportion of patients with eumycetoma had

increased from 32% (13/41) between 1978 and 1989 to 48% (13/27) between 1990 and 2000. Of the 47 eumycetoma cases with known causative organisms, the most common agents were *S. apiospermum* (n=15), *M. mycetomatis* (n=8), and *M. grisea* (n=8). In the northwest of Argentina from 1972 – 1982, four of 39 patients (10%) treated for mycetoma had eumycetoma, all caused by *M. grisea* while in Buenos Aires, from 1989 – 2004, 43 of 76 patients (57%) treated for mycetoma had eumycetoma, most frequently caused by *M. grisea* (n=29).

Mexico reports most cases in America, with more than 4,500 cases and second to Sudan in the world. Most cases (92-95%) are actinomycetomas with a predominance of *Nocardia* species, especially *Nocardia brasiliensis* (70%) and *Actinomyadura madurae* (10%). Regarding eumycetomas, most are caused by black fungi such as *M. mycetomatis*, *M. pseudomycetomatis*, *M. grisea* and *Nigrograna mackinnonii*.

Mycetomas are neglected infections of the poor. They are more than a medical challenge. In rural areas of Africa, Asia and South America mycetomas lead to socio-economic consequences involving the affected patients, their families and the society in general.

More information can be found here:

[www.gaffi.org/wp-content/uploads/Mycetoma-briefing-paper-final-September-2018.pdf](http://www.gaffi.org/wp-content/uploads/Mycetoma-briefing-paper-final-September-2018.pdf)



Typical appearance of eumycetoma on the left foot in a patient from Brazil.



Severe example of eumycetoma in Mexico with extensive subcutaneous and bone involvement.

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### Chromoblastomycosis

After sporotrichosis, chromoblastomycosis or chromomycosis, is the most prevalent implantation fungal infection, and the most common mycosis caused by melanized or brown-pigmented fungi. This disease presents the following characteristics: primary lesion beginning at the site of inoculation; chronic involvement of cutaneous and subcutaneous tissues associated with a granulomatous, purulent, fibrotic tissue formation and a non-protective humoral immune response. The principal etiological agent in Brazil is *F. pedrosoi* (which may include cryptic species, only molecularly identified), followed by sporadic reports of *P. verrucosa* and *E. spinifera*.

In South America, most of the cases of chromoblastomycosis have been described in Brazil. The mean annual incidences of cases of this disease reported in Brazil were 6.4/year (71 cases/11 years) for the state of Paraná (southern region), 5.9/year (325 cases/55 years) for Pará 45 (northern region), 4.3/year (13 cases/3 years) for Maranhão (northeastern region), and 2.6/year (73 cases/28 years) for Rio Grande do Sul (southern region).

Chromoblastomycosis is the predominant implantation mycosis in several countries of Central America and the Caribbean, particularly in the Dominican Republic, Cuba, Panama and Costa Rica. In Mexico, chromoblastomycosis is the third most common implantation mycosis. The number of reported cases exceeds 600, with a predominance in tropical regions, particularly in the Pacific and Gulf of Mexico margins.

Chromoblastomycotic lesions are usually recalcitrant and extremely difficult to eradicate, although early treatment with itraconazole 400mg daily is effective in many patients. Due to its chronicity, lesions may undergo neoplastic transformation leading to skin cancer. Except for small initial lesions that can be cured by surgical removal, chromoblastomycotic lesions constitute a true therapeutic challenge for clinicians and patients.

More information can be found here:

[www.gaffi.org/wp-content/uploads/Chromoblastomycosis-briefing-document-Feb-2018.pdf](http://www.gaffi.org/wp-content/uploads/Chromoblastomycosis-briefing-document-Feb-2018.pdf)



Extensive verrucous lesions on the right forefoot – a case from Brazil.



Extensive, longstanding lesions of chromoblastomycosis from Mexico.

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### Sporotrichosis

Sporotrichosis is the most prevalent and widespread implantation mycosis in the world. It is a subacute to chronic fungal infection caused by several species of the genus *Sporothrix*, a group of thermal dimorphic fungi. Usually, sporotrichosis is an implantation mycosis whose infectious propagules are inoculated from several environmental sources into skin, mucosal or osteoarticular sites. Less frequently, infection may occur by inhalation, resulting in pulmonary disease. In endemic regions, this disease is mainly associated with plant transmission (sapronosis), the main etiologic agents being *S. schenckii* and *S. globosa*.

Although disease occurs worldwide, most cases are reported in tropical and subtropical zones from Latin America, Africa and Asia. Prevalence is not uniform and varies according to the epidemiological pattern of transmission. The highest estimated prevalence rates of infection range from 0.1% to 0.5% in some Latin American countries.

In Mexico large series have been reported (more than 1,000 cases) and, the main etiological agent is *S. schenckii* and in low proportion *S. globosa*. Case reports from several countries have been published, but outbreaks and clusters of cases can occur.

During the last three decades, a new, probable mutant species, *S. brasiliensis*, has emerged in the state of Rio de Janeiro, Brazil. This species is transmitted to humans by infected cats (zoonosis), causing the largest epidemic of sporotrichosis ever reported. This epizootic outbreak continues to expand, affecting

human and feline patients in several Brazilian regions, and neighboring countries. Feline sporotrichosis is unique among infections caused by endemic dimorphic fungi because it is directly transmitted in the yeast phase. The feline lesions typically harbor a high yeast-like fungal burden that can be acquired via cat scratches and bites, by non-traumatic ways, such as a cat's cough or sneezing, and direct contact between patients' integumental barriers and animal secretions. The response to oral itraconazole is excellent, once the diagnosis is established, which can be challenging as both histopathology and culture are not very sensitive.

More information can be found here:

[www.gaffi.org/wp-content/uploads/Sporotrichosis-GAFFI-Fact-sheet-v4-.pdf](http://www.gaffi.org/wp-content/uploads/Sporotrichosis-GAFFI-Fact-sheet-v4-.pdf)



Extensive multi-focal disseminated sporotrichosis in AIDS in Brazil.



Typical lesion of sporotrichosis on the left hand with lymphocutaneous spread up the arm. A case from Brazil.

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### Paracoccidioidomycosis

Among the systemic endemic mycosis observed in the Americas, histoplasmosis, coccidioidomycosis and blastomycosis, paracoccidioidomycosis is one of the most relevant in terms of public health impact, due to its high lung involvement and pulmonary sequelae after antifungal therapy. This disease is autochthonous in Latin America with a high incidence and it may affect travelers from non-endemic areas, years or decades after visiting the etiological agent's natural reservoirs.

Paracoccidioidomycosis is caused by members of the *Paracoccidioides* genus. Like in other systemic endemic mycoses, the lungs are the main portal of entry for the primary infection and most of the infected individuals will not manifest any disease during their lifetime. A minority of patients may evolve with severe clinical signs and symptoms a few weeks or months after infection, as observed in the acute or juvenile type, or years or decades after infection, during the chronic or adult clinical form. Once clinical manifestations are depicted, the natural progression of this mycoses is usually to death. Although the lungs are always involved, dissemination to any organ is common. Because pulmonary involvement of chronic paracoccidioidomycosis is a 'rule in' diagnosis, it is often confused with pulmonary tuberculosis, leading to delayed diagnosis and increasing morbidity and mortality rates.

There is a lack of precise data on paracoccidioidomycosis burden. Estimations of prevalence in Brazil have been made on the basis

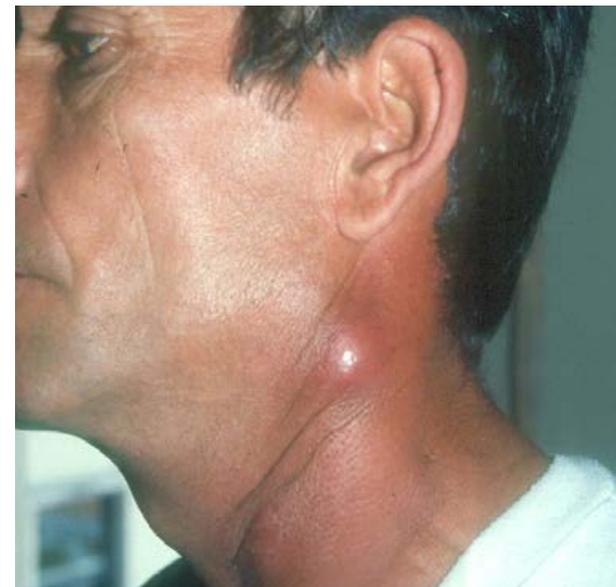
of reported cases series and on hospitalization and mortality data. Overall annual incidence rates of 1-4 cases/100,000 in geographic areas with stable endemicity and 9-40 cases/100,000 in hyperendemic areas. More than that, there is a speculation that at least 10 million habitants of endemic areas have been infected by *Paracoccidioides* sp. Lethality rates are not very high, ranging between 5.2% to 7.6% in three case series from different endemic areas in Brazil.

Endemic zones for paracoccidioidomycosis are present in Colombia, Paraguay, Argentina, and Venezuela. In Mexico, about 100 cases have been reported and there are sporadic reports in some countries of Central America, however cases are not found in any of the Caribbean islands.

The dynamic changing of the hyperendemic areas in Brazil and Argentina seems to be closely associated with human environmental disruption. The high frequency of international travel should raise the suspicion for paracoccidioidomycosis in individuals coming from the endemic areas harboring *Paracoccidioides*. The characteristic long period between infection and emergence of symptoms, makes it mandatory to check for a history of exposure in patients who develop chronic pulmonary symptoms and lung structural abnormalities.

More information can be found here:

[www.gaffi.org/wp-content/uploads/Paracoccidioidomycosis-Briefing-Note.pdf](http://www.gaffi.org/wp-content/uploads/Paracoccidioidomycosis-Briefing-Note.pdf)



Extensive lymph node involvement on the left side of the neck in a rural worker from Brazil.



Typical involvement of the oral mucosa at the sides of the mouth and lips in paracoccidioidomycosis, from Brazil.